

09841025

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(FILE 'HOME' ENTERED AT 11:24:06 ON 26 SEP 2002)

FILE 'REGISTRY' ENTERED AT 11:24:12 ON 26 SEP 2002  
E ZOLPIDEM/CN

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 11:25:03 ON 26 SEP 2002

L2 490 S L1

L3 4 S L2 AND HYDRATE

FILE 'STNGUIDE' ENTERED AT 11:27:25 ON 26 SEP 2002

FILE 'REGISTRY' ENTERED AT 11:28:43 ON 26 SEP 2002  
1 S E4-E5

L4

FILE 'CAPLUS' ENTERED AT 11:31:15 ON 26 SEP 2002

L5 28 S L4

L6 1 S L5 AND HYDRATE

L7 0 S L6 NOT L3

L8 1 S L5 AND MONOHYDRATE

L9 1 S L8 NOT L3

L10 505 S L2 OR L5

L11 3 S L10 AND POLYMORPH?

L12 3 S L11 NOT L3

L13 27 S L5 NOT L12

FILE 'MEDLINE' ENTERED AT 11:36:35 ON 26 SEP 2002

L14 0 S L4

L15 1 S ZOLPIDEM (P) HYDRATE

FILE 'STNGUIDE' ENTERED AT 11:38:42 ON 26 SEP 2002

FILE 'CAPLUS' ENTERED AT 11:40:56 ON 26 SEP 2002

L16 5 S L10 AND HYDRATE?

L17 1 S L16 NOT L3

L18 0 S L17 NOT L11

09841025

> d bib abs kwic

L15 ANSWER 1 OF 1 MEDLINE  
AN 2000216611 MEDLINE  
DN 20216611 PubMed ID: 10755807  
TI Nonselective and selective benzodiazepine receptor agonists--where are we today?.  
AU Mitler M M  
CS Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA 92037, USA.. mitler@scripps.edu  
SO SLEEP, (2000 Feb 1) 23 Suppl 1 S39-47.  
Journal code: 7809084. ISSN: 0161-8105.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200005  
ED Entered STN: 20000518  
Last Updated on STN: 20000518  
Entered Medline: 20000505  
AB Insomnia is problematic for many individuals, causing them to seek treatment. There is a long history of therapies aimed at restoring normal sleep patterns, each having its advantages and disadvantages. This review traces the history of insomnia drug therapies from chloral hydrate and the barbiturates through the benzodiazepines and explores the newest selective benzodiazepine receptor agonists, including zolpidem and zaleplon. The mechanisms of action of the benzodiazepine receptor agonists are compared and contrasted. A pharmacokinetic comparison is presented showing the importance that parameters such as dose, onset of action, lipophilicity, metabolites, half-life, and receptor-binding affinity have on clinical effects. The possible adverse effects of sleep aids are discussed, including residual sedation and psychomotor impairment, daytime anxiety, anterograde amnesia and cognitive impairment, rebound insomnia, and drug tolerance and dependence. Effects on sleep efficiency and staging are also discussed. Recommendations for the primary care physician on the selection of hypnotics are also provided. Benzodiazepine receptor agonists are often appropriate agents in the treatment of insomnia; however, individual drug and patient considerations are important in matching the most appropriate agent to the individual patient. Zolpidem and zaleplon, newer selective benzodiazepine receptor agonists, offer additional treatment options.  
AB . . . normal sleep patterns, each having its advantages and disadvantages. This review traces the history of insomnia drug therapies from chloral hydrate and the barbiturates through the benzodiazepines and explores the newest selective benzodiazepine receptor agonists, including zolpidem and zaleplon. The mechanisms of action of the benzodiazepine receptor agonists are compared and contrasted. A pharmacokinetic comparison is presented. . . of insomnia; however, individual drug and patient considerations are important in matching the most appropriate agent to the individual patient. Zolpidem and zaleplon, newer selective benzodiazepine receptor agonists, offer additional treatment options.

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=> d 1-3 fbib abs

L12 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:798053 CAPLUS  
DN 135:348889  
TI Zolpidem hemitartrate polymorphs for treatment of insomnia  
IN Aronhime, Judith; Dolitzky, Ben-Zion; Kordova, Marco; Leonov, David;  
Meszaros-Sos, Erzebet; Salyi, Szaboles; Schwartz, Anchel; Szabo, Csaba;  
Zavurov, Shlomo  
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,  
Inc.  
SO PCT Int. Appl., 58 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001080857	A1	20011101	WO 2001-US13175	20010424
	WO 2001080857	C2	20020627		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
				US 2000-199298PP	20000424
				US 2000-206025PP	20000522
				US 2000-225364PP	20000814
	US 2002077332	A1	20020620	US 2001-841025	20010424
				US 2000-199298PP	20000424
				US 2000-206025PP	20000522
				US 2000-225364PP	20000814

*this appl*

AB The present invention provides for novel polymorphs of zolpidem hemitartrate and the prepn. of the polymorphs. The zolpidem hemitartrate are prep'd. as hydrates or solvates, e.g., zolpidem hemitartrate methanolate or acetate. For example, 5 g (17.7 mmol) of zolpidic acid was suspended in 50 mL of toluene and 0.15 mL of DMF and the mixt. was cooled to 15-28.degree.. Then, 1.7 mL (23.3 mmol) of thionyl chloride was added into the mixt. at this temp. for 1 h, then it is stirred for 4 h at 35-40.degree.. After formation of acid chloride the thionyl chloride excess was removed by distn. The vol. of the reaction mixt. was adjusted to 50 mL by toluene, then it was cooled to -5-0.degree., and dimethylamine gas was introduced into the reaction mixt. until the pH was 8.5-9.5. Pptn. of zolpidem base started almost immediately. The suspension was cooled to -10-(-12).degree. and mixed for 1 h. The crude product was filtered and washed consecutively with toluene, 5% cooled water soln. of NH4CO3 and cooled water. The product was dried under vacuum to obtain 4.1 g (yield 80%) zolpidem base used in prepn. of hemitartrate polymorphs.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:528011 CAPLUS  
DN 133:344157  
TI Evaluation of the genetic component of variability in CYP3A4 activity: A repeated drug administration method  
AU Ozdemir, Vural; Kalow, Werner; Tang, Bing-Kou; Paterson, Andrew D.; Walker, Scott E.; Endrenyi, Laszlo; Kashuba, Angela D. M.  
CS Departments of Pharmacology and Pharmaceutical Sciences, University of Toronto, Toronto, ON, M5S 1A8, Can.  
SO Pharmacogenetics (2000), 10(5), 373-388  
CODEN: PHMCEE; ISSN: 0960-314X  
PB Lippincott Williams & Wilkins  
DT Journal  
LA English  
AB The CYP3A4 enzyme contributes to the disposition of more than 60 therapeutically important drugs and displays marked person-to-person variability of the catalytic function. However, the extent of genetic contribution to variability in CYP3A4 activity remains elusive. Recently, we showed that a comparison of between- (SDb2) and within-person (SDw2) variances provides an est. of the genetic component of variability in drug disposition. The aim of the present anal. was to assess the genetic control of CYP3A4 activity in vivo. A computerized literature search was

conducted covering 1966 to Sept. 1999 to identify studies reporting repeated administration of CYP3A4 substrates. The genetic contribution (rGC) to disposition of each CYP3A4 substrate was obtained by the formula (SDB2 - SDw2)/SDB2. The rGC values approaching 1.0, point to overwhelming genetic control, whereas those close to zero suggest that environmental factors dominate. A total of 16 studies with 10 different CYP3A4 substrates were identified (n = 161 subjects). The rGC for hepatic CYP3A4 activity as measured by midazolam plasma clearance or the erythromycin breath test was 0.96 (0.92-0.98) (95% CI) and 0.89 (0.65-0.98), resp. (P < 0.05). The point ests. of rGC for composite (hepatic + intestinal) CYP3A4 activity measured after oral administration of cyclosporine, ethinylestradiol, ethylmorphine, nifedipine and nitrendipine, ranged from 0.66-0.98 (median: 0.83) (P < 0.05). Cyclosporine data suggested a higher genetic control of CYP3A4 at night than during the day. These data indicate that further mol. genetic investigations are warranted to identify genetic variants at CYP3A4 or elsewhere in the genome which contribute to regulation of CYP3A4 activity.

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

AN 1999:310588 CAPLUS

DN 131:96890

TI Pharmacologic and behavioral responses of inbred C57BL/6J and Strain 129/SvJ mouse lines

AU Homanics, Gregg E.; Quinlan, Joseph J.; Firestone, Leonard L.

CS Departments of Anesthesiology/Critical Care Medicine and Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SO Pharmacology, Biochemistry and Behavior (1999), 63(1), 21-26

CODEN: PBBHAU; ISSN: 0091-3057

PB Elsevier Science Inc.

DT Journal

LA English

AB Gene-targeting technol. is creating an explosion in the no. of animals available with single gene mutations that affect the function of the central nervous system. Most gene-targeted mice are produced on a mixed genetic background of C57BL/6J and substrains of Strain 129. Understanding the behavioral characteristics and responses to various drugs of these parental strains is vital to interpreting data from gene-targeted mice. We directly compared C57BL/6J and Strain 129/SvJ mouse lines on several behavioral paradigms and in response to several hypnotic and anesthetic drugs. Compared to Strain 129/SvJ mice, C57BL/6J animals are more sensitive to the hypnotic effects of midazolam, zolpidem, and propofol, less sensitive to etomidate and ethanol, and do not differ in sensitivity to Ro15-4513 or pentobarbital. These strains do not differ in their sensitivity to the motor ataxic effects of the volatile anesthetics enflurane or halothane. However, Strain 129/SvJs are more sensitive to the immobilizing effects of halothane but not enflurane. Motor coordination differs initially, but with repeated testing strain differences are no longer apparent. Strain 129/SvJ mice are more anxious on the elevated plus maze and open-field activity assays. Thus, these mouse strains harbor polymorphisms that influence some, but not all, traits of interest to behavioral neuroscientists.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 11:24:06 ON 26 SEP 2002)

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E ZOLPIDEM/CN

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FILE 'CAPLUS' ENTERED AT 11:25:03 ON 26 SEP 2002

L2 490 S L1

L3 4 S L2 AND HYDRATE

FILE 'STNGUIDE' ENTERED AT 11:27:25 ON 26 SEP 2002

FILE 'REGISTRY' ENTERED AT 11:28:43 ON 26 SEP 2002  
1 S E4-E5

L4

FILE 'CAPLUS' ENTERED AT 11:31:15 ON 26 SEP 2002

L5 28 S L4

L6 1 S L5 AND HYDRATE

L7 0 S L6 NOT L3

09841025

L8 1 S L5 AND MONOHYDRATE  
L9 1 S L8 NOT L3  
L10 505 S L2 OR L5  
L11 3 S L10 AND POLYMORPH?  
L12 3 S L11 NOT L3

=> s 15 not 112  
L13 27 L5 NOT L12

=> d 1-3 bib abs

L13 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:408517 CAPLUS  
DN 137:741  
TI Inhibitors of ABC drug transporters at the blood-brain barrier for  
increasing brain concns. of central nervous system-active agents  
IN Schoenhard, Grant L.  
PA Pain Therapeutics, Inc., USA  
SO PCT Int. Appl., 143 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 13

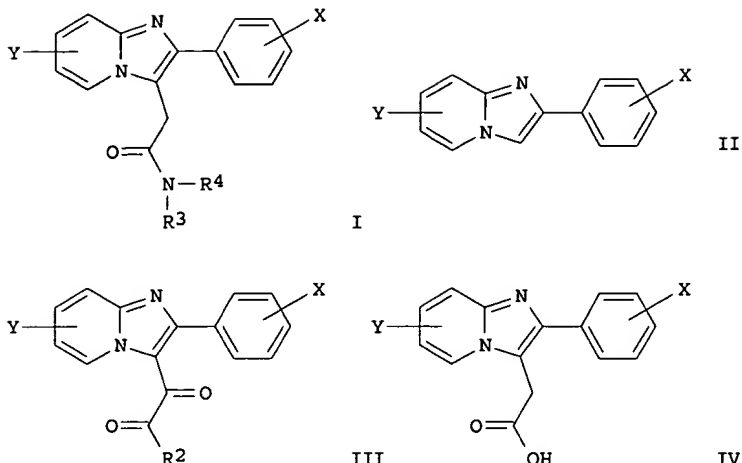
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002041884	A2	20020530	WO 2001-US45367	20011030
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 6011004	A	20000104	US 1996-768221	19961217
	AU 9947399	A1	19991028	AU 1999-47399	19990906
	AU 2002039427	A5	20020603	AU 2002-39427	20011030
PRAI	US 2000-244482P	P	20001030		
	US 2000-245110P	P	20001101		
	US 2000-246235P	P	20001102		
	US 1990-612847	B1	19901113		
	US 1993-153796	A1	19931117		
	AU 1995-32769	A3	19950718		
	WO 2001-US45367	W	20011030		

OS MARPAT 137:741

AB The invention relates to inhibitors of drug transporters of the ABC protein superfamily, particularly transporters present at the blood brain barrier. ABC transporter inhibitors identified according to the invention increase brain concns. of CNS-active agents. Such inhibitors increase the influx into the brain and/or reduce the efflux from the brain of such CNS-active agents.

L13 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:47557 CAPLUS  
DN 136:102382  
TI A process for the preparation of 2-phenyl-imidazo[1,2-a]pyridine-3-acetamides  
IN Castaldi, Graziano  
PA Dinamite Dipharma S.P.A. (In Abbreviated Form Dipharma S.P.A.), Italy  
SO Eur. Pat. Appl., 18 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1172364	A1	20020116	EP 2001-116016	20010702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2002019528	A1	20020214	US 2001-902616	20010712
	US 6384226	B2	20020507		
	JP 2002167385	A2	20020611	JP 2001-212175	20010712
PRAI	IT 2000-MI1591	A	20000714		
OS	CASREACT 136:102382; MARPAT 136:102382				
GI					



AB A process for the prepn. of 2-phenyl-imidazo[1,2-a]pyridine-3-acetamides (I; X = H, halo, C1-4 alkyl, C1-6 alkoxy, CF<sub>3</sub>, MeS, NO<sub>2</sub>, MeSO<sub>2</sub>; Y = H, halo, C1-4 alkyl; R<sub>3</sub>, R<sub>4</sub> = H, C1-5 alkyl, allyl, propargyl, C3-6 cycloalkyl, CH<sub>2</sub>Ph, Ph) comprises the reaction of a 2-phenyl-imidazo[1,2-a]pyridine (II; X, Y = same as above) with an oxalic ester reactive deriv. of formula R<sub>1</sub>COCOR<sub>2</sub> (R<sub>1</sub> = halo, a carboxy-activating group; R<sub>2</sub> = C1-6 alkoxy or phenoxy both optionally substituted with C1-6 alkyl or alkoxy, C1-6 alkylamino, arylamino), followed by reducing the carbonyl group of the resulting glyoxalate esters (III; R<sub>2</sub> = same as above) and reacting the resulting carboxylic acids (IV; X, Y = same as above) with an amine of formula NHR<sub>3</sub>R<sub>4</sub>. This process provides an efficient, convenient route for the prepn. of 2-phenylimidazo[1,2-a]pyridine-3-acetamides, in particular zolpidem. All known synthesis of zolpidem used either reagents com. available with difficulty, toxic reagents, or industrially unsuitable procedures due to low yields and/or products with poor purity which should undergo repeated purifn. procedures. Under the best operative conditions, this method gives zolpidem of suitable quality and in yields above 80%, starting from imidazopyridine. Thus, chlorination of potassium monoethyl oxalate with POCl<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> at .apprx.30.degree. for 4-6 h followed by acylation of 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine with the resulting oxalic acid chloride Et ester in the presence of Et<sub>3</sub>N under reflux for 1 h gave 97.5% Et 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine-3-glyoxalate (V). Sapon. of V with NaOH in aq. EtOH under reflux, followed by condensation with hydrazine under reflux for 14 h and distn. in the presence of KOH at 122-14.degree. under refluxing until N evolution ceased gave, after acidification with AcOH, 96.5% 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine-3-acetic acid (VI). Chlorination of VI with oxalyl chloride in CH<sub>2</sub>Cl<sub>2</sub> under reflux for 30 min and amidation with dimethylamine hydrochloride at room temp. for 1 h gave zolpidem which was converted into zolpidem oxalate.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2002 ACS

AN 2001:780683 CAPLUS

DN 135:335156

TI Modified-release formulations containing a hypnotic agent

IN Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria

PA Synthon B.V., Neth.

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001078725	A2	20011025	WO 2001-NL299	20010412
	WO 2001078725	A3	20011220		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-196939P P 20000413

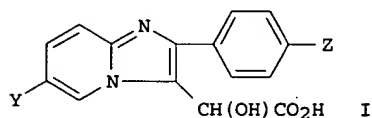
AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

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=> d bib abs kwic

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS  
 AN 2000:686287 CAPLUS  
 DN 133:252434  
 TI Imidazopyridine derivatives and process for making them  
 IN Ettema, Gerrit Jan Bouke; Lemmens, Jacobus Maria; Peters, Theodorus  
 Hendricus Antonius; Picha, Frantisek  
 PA Synthon B.V., Neth.  
 SO Eur. Pat. Appl., 15 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1038875	A2	20000927	EP 1999-203478	19991022
	EP 1038875	A3	20010912		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6281360	B1	20010828	US 2000-512789	20000225
	NL 1014634	C1	20000803	NL 2000-1014634	20000313
	WO 2000058310	A1	20001005	WO 2000-NL171	20000313
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1163241	A1	20011219	EP 2000-913159	20000313
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-126494P	P	19990325		
	EP 1999-203478	A	19991022		
	US 1999-449974	A	19991126		
	WO 2000-NL171	W	20000313		
OS	CASREACT 133:252434; MARPAT 133:252434				
GI					



AB Imidazopyridines I (Y, Z = lower alkyl) were prepd. by reaction of 6-alkyl-2-(p-alkylphenyl)imidazo[1,2-a]pyridines with glyoxylic acid or its acetal. Thus, 22 g of 6-methyl-2-p-tolylimidazo[1,2-a]pyridine was suspended in 100 mL of dichloroethene, 10 g of glyoxylic acid monohydrate was added, and the mixt. was heated to reflux for 1.5 h to give 28 g of I (Y = Z = Me) with a purity of 97.9%.

AB Imidazopyridines I (Y, Z = lower alkyl) were prepd. by reaction of 6-alkyl-2-(p-alkylphenyl)imidazo[1,2-a]pyridines with glyoxylic acid or its acetal. Thus, 22 g of 6-methyl-2-p-tolylimidazo[1,2-a]pyridine was suspended in 100 mL of dichloroethene, 10 g of glyoxylic acid monohydrate was added, and the mixt. was heated to reflux for 1.5 h to give 28 g of I (Y = Z = Me) with a purity of 97.9%.

IT 82626-48-OP, Zolpidem 99294-93-6P, Zolpidem hemitartrate  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

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=> d 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 82626-48-0 REGISTRY

CN Imidazo[1,2-a]pyridine-3-acetamide, N,N,6-trimethyl-2-(4-methylphenyl)-  
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN SL 80-0750

CN Zolpidem

FS 3D CONCORD

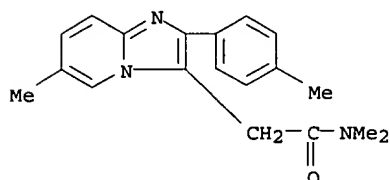
MF C19 H21 N3 O

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST,  
CIN, CSCHM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,  
EMBASE, IPA, MEDLINE, MRCK\*, NIOSHTIC, PHAR, PROMT, RTECS\*, SYNTHLINE,  
TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

489 REFERENCES IN FILE CA (1962 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

491 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s e4-e5

1 "ZOLPIDEM HEMITARTRATE"/CN

1 "ZOLPIDEM TARTRATE"/CN

L4 1 ("ZOLPIDEM HEMITARTRATE"/CN OR "ZOLPIDEM TARTRATE"/CN)

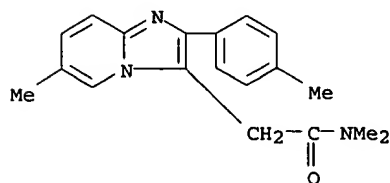
=> d scan

L4 1 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Imidazo[1,2-a]pyridine-3-acetamide, N,N,6-trimethyl-2-(4-methylphenyl)-,  
(2R,3R)-2,3-dihydroxybutanedioate (2:1) (9CI)

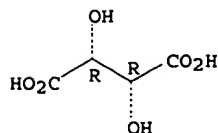
MF C19 H21 N3 O . 1/2 C4 H6 O6

CM 1



CM 2

Absolute stereochemistry.



09841025

09841025

=> d 1-4 bib abs kwic

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:780683 CAPLUS  
DN 135:335156  
TI Modified-release formulations containing a hypnotic agent  
IN Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria  
PA Synthon B.V., Neth.  
SO PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001078725	A2	20011025	WO 2001-NL299	20010412
	WO 2001078725	A3	20011220		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2000-196939P P 20000413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

IT 50-35-1, Thalidomide 2809-21-4 4291-63-8, Cladribine 5630-53-5, Tibolone 5633-20-5, Oxybutynin 9004-34-6, Cellulose, biological studies 12794-10-4D, Benzodiazepine, derivs. 24584-09-6, Dexrazoxane 42399-41-7, Diltiazem 43200-80-2, Zopiclone 51803-78-2, Nimesulide 54024-22-5, Desogestrel 56180-94-0, Acarbose 59729-33-8, Citalopram 61869-08-7, Paroxetine 68291-97-4, Zonisamide 68693-11-8, Modafinil 71620-89-8, Reboxetine 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75706-12-6, Leflunomide 75887-54-6, Artemotil 76963-41-2, Nizatidine 79902-63-9, Simvastatin 80125-14-0, Remoxipride 82626-48-0, Zolpidem 85650-52-8, Mirtazapine 88150-42-9, Amlodipine 91374-21-9 93413-69-5, Venlafaxine 96829-58-2, Orlistat 99294-93-6, Zolpidem tartrate 103188-50-7 104632-26-0, Pramipexole 105816-04-4, Nateglidine 106133-20-4, Tamsulosin 106266-06-2, Risperidone 107868-30-4, Exemestane 111025-46-8, Pioglitazone 111974-69-7, Quetiapine 112809-51-5, Letrozole 113665-84-2, Clopidogrel 113806-05-6, Olopatadine 115256-11-6, Dofetilide 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 124937-51-5, Tolterodine 130209-82-4, Latanoprost 132539-06-1, Olanzapine 133040-01-4, Eprosartan 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 139481-59-7, Candesartan 144034-80-0, Rizatriptan 144701-48-4,

09841025

Telmisartan 146939-27-7, Ziprasidone 151319-34-5, Zaleplon  
185243-69-0, Etanercept 299397-15-2 299397-16-3 299397-18-5  
299397-19-6 299397-20-9 299397-23-2 299397-24-3 299397-25-4  
369371-24-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(modified-release formulations contg. hypnotic agent)

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 2001:338762 CAPLUS

DN 134:362292

TI Methods of determining individual hypersensitivity to a pharmaceutical  
agent from gene expression profile

IN Farr, Spencer

PA Phase-1 Molecular Toxicology, USA

SO PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032928	A2	20010510	WO 2000-US30474	20001103
	WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein  
arrays, and devices that may be used to det. the hypersensitivity of  
individuals to a given agent, such as drug or other chem., in order to  
prevent toxic side effects. In one embodiment, methods of identifying  
hypersensitivity in a subject by obtaining a gene expression profile of  
multiple genes assocd. with hypersensitivity of the subject suspected to  
be hypersensitive, and identifying in the gene expression profile of the  
subject a pattern of gene expression of the genes assocd. with  
hypersensitivity are disclosed. The gene expression profile of the  
subject may be compared with the gene expression profile of a normal  
individual and a hypersensitive individual. The gene expression profile  
of the subject that is obtained may comprise a profile of levels of mRNA  
or cDNA. The gene expression profile may be obtained by using an array of  
nucleic acid probes for the plurality of genes assocd. with  
hypersensitivity. The expression of the genes predetd. to be assocd. with  
hypersensitivity is directly related to prevention or repair of toxic  
damage at the tissue, organ or system level. Gene databases arrays and  
app. useful for identifying hypersensitivity in a subject are also  
disclosed.

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies  
50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8,  
Prednisolone 50-28-2, Estradiol, biological studies 50-44-2,  
6-Thiopurine 50-48-6, Amitriptyline 50-55-5, Reserpine 50-76-0,  
Actinomycin D 50-78-2, Aspirin 51-06-9, Procainamide 51-21-8,  
Fluorouracil 51-34-3, Scopolamine 51-48-9, Levothyroxine, biological  
studies 51-49-0, Dextrothyroxine 51-55-8, Atropine, biological studies  
51-75-2, Mechlorethamine 52-01-7, Spironolactone 52-53-9, Verapamil  
52-67-5, Penicillamine 52-86-8, Haloperidol 53-03-2, Prednisone  
53-06-5, Cortisone 53-19-0, Mitotane 53-33-8, Paramethasone 53-86-1,  
Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-31-9,  
Furosemide 54-36-4, Metyrapone 54-85-3, Isoniazid 55-63-0,  
Nitroglycerin 55-65-2, Guanethidine 55-98-1, Busulfan 56-54-2,  
Quinidine 56-75-7, Chloramphenicol 57-22-7, Vincristine 57-41-0,  
Phenytoin 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-66-9,  
Probenecid 57-83-0, Progestin, biological studies 57-96-5,  
Sulfipyrazole 58-05-9, Leucovorin 58-14-0, Pyrimethamine 58-32-2,  
Dipyridamole 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9,  
Theophylline, biological studies 58-61-7, Adenosine, biological studies  
58-74-2, Papaverine 58-93-5, Hydrochlorothiazide 58-94-6, Thiazide  
59-05-2, Methotrexate 59-42-7, Phenylephrine 59-43-8, Thiamine,  
biological studies 59-92-7, Levodopa, biological studies 59-99-4,  
Neostigmine 60-40-2, Mecamylamine 60-54-8, Tetracycline 60-79-7,  
Ergonovine 60-87-7, Promethazine 61-32-5, Methicillin 61-72-3,  
Cloxacillin 64-75-5, Tetracycline hydrochloride 64-77-7, Tolbutamide

64-86-8, Colchicine 65-23-6, Pyridoxine 66-79-5, Oxacillin 66-97-7, Psoralen 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-68-5, Dimethyl sulfoxide, biological studies 68-22-4D, Norethindrone, mixt. with ethinyl estradiol 68-41-7, Cycloserine 68-88-2, Hydroxyzine 69-53-4, Ampicillin 69-72-7, biological studies 69-89-6, Xanthine 73-24-5, 6-Aminopurine, biological studies 73-31-4, Melatonin 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-36-1, Chlorthalidone 78-44-4, Carisoprodol 80-08-0, Dapsone 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 82-92-8, Cyclizine 82-95-1, Buclizine 83-43-2, Methylprednisolone 83-73-8, Iodoquinol 83-89-6, Quinacrine 83-98-7, Orphenadrine 86-54-4, Hydralazine 89-57-6, Mesalamine 90-34-6, Primaquine 90-82-4, Pseudoephedrine 91-64-5, Coumarin 92-13-7, Pilocarpine 92-84-2, Phenothiazine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 94-36-0, Benzoyl peroxide, biological studies 94-78-0, Phenazopyridine 95-25-0, Chlorzoxazone 96-64-0, Soman 97-77-8, Disulfiram 99-66-1, Valproic acid 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies 101-31-5, Hyoscyamine 103-90-2, Acetaminophen 113-18-8, Ethchlorvynol 113-42-8, Methylegonovine 113-45-1, Methylphenidate 114-07-8, Erythromycin 114-86-3, Phenformin 118-42-3, Hydroxychloroquine 122-09-8, Phentermine 123-56-8, Succinimide 123-63-7, Paraldehyde 124-94-7, Triamcinolone 125-29-1, Hydrocodone 125-33-7, Primidone 125-64-4, Methypylon 125-71-3, Dextromethorphan 125-84-8, Aminogluthethimide 126-07-8, Griseofulvin 126-52-3, Ethinamate 127-07-1, Hydroxyurea 127-69-5, Sulfisoxazole 128-13-2, Ursodiol 130-95-0, Quinine 132-17-2, Benztropine 133-10-8, Sodium p-aminosalicylate 137-58-6, Lidocaine 138-56-7, Trimethobenzamide 144-11-6, Trihexyphenidyl 147-52-4, Nafcillin 147-94-4, AraC 148-82-3, Melfalan 154-21-2, Lincomycin 154-42-7, Thioguanine 154-93-8, Carmustine 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-50-0, Propantheline 299-42-3, Ephedrine 300-62-9D, Amphetamine, mixed 300-62-9D, Amphetamine, mixed salts 302-17-0, Chloral hydrate 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine 305-03-3, Chlorambucil 315-30-0, Allopurinol 321-64-2, Tacrine 346-18-9, Polythiazide 361-37-5, Methysergide 363-24-6, Dinoprostone 364-62-5, Metoclopramide 378-44-9, Betamethasone 389-08-2, Nalidixic acid 395-28-8, Isoxsuprine 439-14-5, Diazepam 443-48-1, Metronidazole 446-86-6, Azathioprine 456-59-7, Cyclandelate 461-72-3, Hydantoin 463-04-7, Amyl nitrite 469-62-5, Propoxyphene 474-25-9, Chenodiol 480-30-8, Dichloralphenazone 484-23-1, Dihydralazine 503-01-5, Isometheptene 512-15-2, Cyclopentolate 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 526-36-3, Xylometazoline 536-33-4, Ethionamide 541-15-1, Levocarnitine 546-88-3, Acetohydroxamic acid 555-30-6, Methyl dopa 564-25-0, Doxycycline 569-65-3, Meclizine 577-11-7, Docusate sodium 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 603-50-9, Bisacodyl 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 671-16-9, Procarbazine 672-87-7, Metyrosine 674-38-4, Bethanechol 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 745-65-3, Alprostadil 791-35-5, Chlophedianol 797-63-7, Levonorgestrel 797-64-8D, L-Norgestrel, ethinyl estradiol mixt. 846-49-1, Lorazepam 846-50-4, Temazepam 911-45-5, Clomiphene 915-30-0, Diphenoxylate 962-58-3, Diazoxon 968-93-4, Testolactone 972-02-1, Diphenidol 990-73-8, Fentanyl citrate 1134-47-0, Baclofen 1143-38-0, Anthralin 1321-13-7, Potassium aminobenzoate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1404-04-2, Neomycin 1404-04-2D, Neomycin, mixt. with polymyx/HC 1404-90-6, Vancomycin 1406-05-9, Penicillin 1491-59-4, Oxymetazoline 1622-61-3, Clonazepam 1953-02-2, Tiopronin 1977-10-2, Loxapine 2152-34-3, Pemoline 2152-44-5, Betamethasone valerate 2447-57-6, Sulfadoxine 2451-01-6, Terpin hydrate 2609-46-3, Amiloride 2809-21-4 2998-57-4, Estramustine 3116-76-5, Dicloxacillin 3313-26-6, Thiothixene 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3737-09-5, Disopyramide 3778-73-2, Iphosphamide  
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 4499-40-5, Oxtriphylline, biological studies 4618-18-2, Lactulose 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin 5051-62-7, Guanabenz 5543-57-7, (s)-Warfarin 5633-20-5, Oxybutynin 5786-21-0, Clozapine 6190-39-2, Dihydroergotamine mesylate 6493-05-6, Pentoxifylline 6621-47-2, Perhexiline 7020-55-5, Clidinium 7235-40-7, Beta carotene 7261-97-4, Dantrolene 7416-34-4, Molindone 7439-93-2, Lithium, biological studies 7447-40-7, Potassium chloride, biological studies 7481-89-2, Zalcitabine 7487-88-9, Magnesium sulfate, biological studies 7648-98-8, Ambenonium 7681-11-0, Potassium iodide, biological studies 7681-93-8, Natamycin 7683-59-2, Isoproterenol 8029-99-0, Paregoric

8049-47-6, Pancreatin 8050-81-5, Simethicone 8063-07-8, Kanamycin  
 8067-24-1, Ergoloid mesylates 9001-27-8, Blood-coagulation factor VIII  
 9001-75-6, Pepsin 9004-10-8, Insulin, biological studies 9004-67-5,  
 Methyl cellulose 9005-49-6, Enoxaparin, biological studies 9007-92-5,  
 Glucagon, biological studies 9039-53-6, Urokinase 9046-56-4, Ancrod  
 10118-90-8, Minocycline 10238-21-8, Glyburide 10262-69-8, Maprotiline  
 10540-29-1, Tamoxifen 11041-12-6, Cholestyramine 11056-06-7, Bleomycin  
 11111-12-9, Cephalosporin 12174-11-7, Attapulgit 12244-57-4, Gold  
 sodium thiomalate 12650-69-0, Mupirocin 12794-10-4D, Benzodiazepine,  
 derivs. 13010-47-4, Lomustine 13292-46-1, Rifampin 13311-84-7,  
 Flutamide 13392-28-4, Rimantadine 13647-35-3, Trilostane 14028-44-5,  
 Amoxapine 14124-50-6 14611-51-9, Selegiline 14769-73-4, Levamisole  
 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate  
 15301-69-6, Flavoxate 15307-86-5, Diclofenac 15663-27-1, Cisplatin  
 15686-71-2, Cephalixin 15687-27-1, Ibuprofen 15722-48-2, Olsalazine  
 16051-77-7, Isosorbide mononitrate 16068-46-5, Potassium phosphate  
 16110-51-3, Cromolyn 16590-41-3, Naltrexone 16679-58-6, Desmopressin  
 17230-88-5, Danazol 17784-12-2, Sulfacytine 18323-44-9, Clindamycin  
 18559-94-9, Albuterol 18883-66-4, Streptozocin 19216-56-9, Prazosin  
 19794-93-5, Trazodone 20537-88-6, Amifostine 20830-75-5, Digoxin  
 20830-81-3, Daunomycin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine  
 22204-53-1, Naproxen 22232-71-9, Mazindol 23031-32-5, Terbutaline  
 sulfate 23214-92-8, Doxorubicin 23288-49-5, Probuco 25322-68-3,  
 Polyethylene glycol 25451-15-4, Felbamate 25614-03-3, Bromocriptine  
 25812-30-0, Gemfibrozil 26652-09-5, Ritodrine 26787-78-0, Amoxicillin  
 26807-65-8, Indapamide 26839-75-8, Timolol 27203-92-5, Tramadol  
 27262-47-1, Levobupivacaine 27686-84-6, Masoprocol 28395-03-1,  
 Bumetanide 28657-80-9, Cinoxacin 28782-42-5, Difenoxin 28860-95-9,  
 Carbidopa 28911-01-5, Triazolam 28981-97-7, Alprazolam 29094-61-9,  
 Glipizide 29110-47-2, Guanfacine 29122-68-7, Atenolol 30516-87-1,  
 Zidovudine 31441-78-8, Mercaptopurine 31677-93-7, Bupropion  
 hydrochloride 31828-71-4, Mexiletine 31883-05-3, Moricizine  
 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 33419-42-0, Etoposide  
 34089-81-1, Sodium ferric gluconate 35189-28-7, Norgestimate  
 36322-90-4, Piroxicam 36505-84-7, Buspirone 36791-04-5, Ribavirin  
 38304-91-5, Minoxidil 40180-04-9, Tienilic acid 40580-59-4, Guanadrel  
 41575-94-4, Carboplatin 41708-72-9, Tocainide 42399-41-7, Diltiazem  
 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 50679-08-8, Terfenadine  
 50925-79-6, Colestipol 50972-17-3, Bacampicillin 51022-71-0, Nabilone  
 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol  
 51481-61-9, Cimetidine 53179-11-6, Loperamide 53230-10-7, Mefloquine  
 53608-75-6, Pancrelipase 53714-56-0, Leuprolide 53994-73-3, Cefaclor  
 54024-22-5, Desogestrel 54063-53-5, Propafenone 54143-56-5, Flecainide  
 acetate 54182-58-0, Sucralfate 54350-48-0, Etretinate 54573-75-0,  
 Doxercalciferol 54910-89-3, Fluoxetine 55142-85-3, Ticlopidine  
 55268-75-2, Cefuroxime 55985-32-5, Nicardipine 56420-45-2, Epirubicin  
 58001-44-8 58581-89-8, Azelastine 59122-46-2, Misoprostol  
 59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporine  
 A 60142-96-3, Gabapentin 60205-81-4, Ipratropium 61489-71-2,  
 Menotropin 61718-82-9, Fluvoxamine maleate 61869-08-7, Paroxetine  
 62571-86-2, Captopril 63585-09-1, Fosarnet sodium 63590-64-7,  
 Terazosin 64952-97-2, Latamoxef 65141-46-0, Nicorandil 65277-42-1,  
 Ketoconazole 66085-59-4, Nimodipine 66104-22-1, Pergolide  
 66357-35-5, Ranitidine 66376-36-1, Alendronate 67227-57-0, Fenoldopam  
 mesylate 68475-42-3, Anagrelide 68844-77-9, Astemizole 69049-73-6,  
 Nedocromil 69123-98-4, Fialuridine 69655-05-6, Didanosine  
 70359-46-5, Brominide tartrate 70989-04-7, S-Mephenytoin 71320-77-9,  
 Moclobemide 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3,  
 Carvedilol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8,  
 Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6,  
 Leflunomide 75847-73-3, Enalapril 76470-66-1, Loracarbef 76547-98-3,  
 Lisinopril 76568-02-0, Flosequinan 76584-70-8 76824-35-6, Famotidine  
 76932-56-4, Nafarelin 76963-41-2, Nizatidine 78110-38-0, Aztreonam  
 78628-80-5, Terbinafine hydrochloride 79516-68-0, Levocabastine  
 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin  
 80125-14-0, Remoxipride 80474-14-2, Fluticasone propionate 81093-37-0,  
 Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin  
 81669-57-0, Anistreplase 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin  
 82626-48-0, Zolpidem 82834-16-0, Perindopril 83366-66-9,  
 Nefazodone 83799-24-0, Fexofenadine 83881-51-0, Cetirizine  
 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84449-90-1,  
 Raloxifene 84625-61-6, Itraconazole 85441-61-8, Quinapril  
 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5,  
 Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88040-23-7,  
 Cefepime 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89778-26-7,  
 Toremfene 90566-53-3, Fluticasone 91714-94-2, Bromfenac 92665-29-7,  
 Cefprozil 93390-81-9, Fosphenytoin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)  
(methods of detg. individual hypersensitivity to a pharmaceutical agent  
from gene expression profile)

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:875749 CAPLUS  
DN 134:33001  
TI Alkali metal and alkaline-earth metal salts of acetaminophen  
IN Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max;  
Martellucci, Stephen A.  
PA McNeill-PPC, Inc., USA  
SO U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 987,210, abandoned.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6160020	A	20001212	US 1998-100284	19980619
	WO 9966919	A1	19991229	WO 1999-US13064	19990609
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9943380	A1	20000110	AU 1999-43380	19990609
PRAI	US 1996-771176	B2	19961220		
	US 1997-987210	B2	19971209		
	US 1998-100284	A	19980619		
	WO 1999-US13064	W	19990609		

AB Isolated salts of acetaminophen are disclosed. Alkali metal and alk.-earth metal salts of acetaminophen are formed by reacting the free acid of acetaminophen with the corresponding metal hydroxide and then immediately isolating the resulting salt. These salts have been found to be more water sol. and less bitter in taste than the free acid form of acetaminophen. The isolated salts may also be combined with other active ingredients. A tablet contained calcium acetaminophen 368.23, chlorpheniramine maleate 2, microcryst. cellulose 520.77, silica 4.5, and Mg stearate 4.5 mg.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-78-2, Acetyl salicylic acid 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 53-86-1, Indomethacin 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine 59-33-6, Pyrilamine 59-42-7, Phenylephrine 60-87-7, Promethazine 68-88-2, Hydroxyzine 73-31-4, Melatonin 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-22-5, Caramiphen 77-23-6, Carbetapentane 86-22-6, Brompheniramine 90-82-4, Pseudoephedrine 91-81-6, Tripeleminamine 93-14-1, Guaifenesin 104-31-4, Benzonatate; 113-92-8 125-29-1, Hydrocodone 125-71-3, Dextromethorphan 128-62-1, Noscapine 129-03-3, Cyproheptadine 132-21-8, Dexbrompheniramine 299-42-3, Ephedrine; 317-34-0, Aminophylline 364-62-5, Metoclopramide 466-99-9, Hydromorphone 471-34-1, Calcium carbonate, biological studies 486-12-4, Triprolidine 554-10-9, 3-Iodo-1,2-propanediol 562-10-7, Doxylamine 586-06-1, Metaproterenol 606-04-2, Pamabrom. 616-91-1 642-72-8, Benzydamine 791-35-5, Chlophedianol 915-30-0, Diphenoxylate 2451-01-6, Terpin hydrate 3572-43-8, Bromhexine 3964-81-6, Azatadine 5104-49-4, Flurbiprofen 7020-55-5, Clidinium 7683-59-2, Isoprenaline 8050-81-5, Simethicone 12125-02-9, Ammonium chloride, biological studies 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16958-94-4 18053-31-1, Fominoben 18559-94-9, Albuterol; 18683-91-5, Ambroxol 21645-51-2, Aluminum hydroxide, biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutaline 25523-97-1, Dexchlorpheniramine 27203-92-5, Tramadol 29679-58-1, Fenoprofen 29975-16-4, Estazolam 30392-40-6, Bitolterol 33005-95-7, Tiaprofenic acid 34580-13-7, Ketotifen 35719-43-8 36322-90-4, Piroxicam 36950-96-6, Cicloprofen 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 50679-08-8, Terfenadine 51481-61-9, Cimetidine 51803-78-2, Nimesulide 53179-11-6, Loperamide; 53716-49-7, Carprofen 54182-58-0, Sucralfate 57644-54-9, Bismuth subcitrate 61869-07-6, Domiodol 66357-35-5, Ranitidine 68844-77-9, Astemizole 71125-38-7, Meloxicam 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74978-16-8, Magaldrate 75970-99-9, Norastemizole

09841025

76824-35-6, Famotidine 76963-41-2, Nizatidine 79794-75-5, Loratidine  
80937-31-1, Flosulide 81098-60-4, Cisapride 82626-48-0,  
Zolpidem 83799-24-0, Fexofenadine; 83881-51-0, Cetirizine  
86181-42-2, Temelastine 87848-99-5, Acrivastine 169590-42-5, Celecoxib  
180200-68-4 209967-48-6 209967-50-0 209967-51-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(oral compns. contg. acetaminophen metal salt and other actives)

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 1999:819235 CAPLUS

DN 132:54898

TI Pharmaceutical composition containing a salt of acetaminophen and at least  
one other active ingredient

IN Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max;  
Martellucci, Stephen A.

PA Mcneil-PPC, Inc., USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9966919	A1	19991229	WO 1999-US13064	19990609
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6160020	A	20001212	US 1998-100284	19980619
	AU 9943380	A1	20000110	AU 1999-43380	19990609
PRAI	US 1998-100284	A	19980619		
	US 1996-771176	B2	19961220		
	US 1997-987210	B2	19971209		
	WO 1999-US13064	W	19990609		

AB This invention relates to pharmaceutical compns. comprising an alkali or alk.-earth metal salt of acetaminophen and at least one other active ingredient selected from the group consisting of analgesics, decongestants, expectorants, antitussives, antihistamines, gastrointestinal agents, diuretics, bronchodilators and mixts. thereof. The acetaminophen salts have both improved aq. soly. and a less bitter taste than the free acid form of acetaminophen. A tablet contained acetaminophen calcium salt 368.23, chlorpheniramine maleate 2, microcryst. cellulose 520.77, Cab-O-Sil M5 4.5, and Mg stearate 4.5 mg.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-78-2, Acetylsalicylic acid 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 53-86-1, Indomethacin 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine 59-33-6, Pyrilamine 59-42-7, Phenylephrine 60-87-7, Promethazine 68-88-2, Hydroxyzine 73-31-4 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-22-5, Caramiphen 77-23-6, Carbetapentane 86-22-6, Brompheniramine 90-82-4, Pseudoephedrine 91-81-6, Tripeleminamine 93-14-1, Guaifenesin 103-90-2 104-31-4, Benzonatate 113-92-8, Chlorpheniramine maleate 125-29-1, Hydrocodone 125-69-9, Dextromethorphan hydrobromide 125-71-3, Dextromethorphan 128-62-1, Noscapine 129-03-3, Cyproheptadine 132-21-8, Dexbrompheniramine 147-24-0, Diphenhydramine hydrochloride 299-42-3, Ephedrine 317-34-0, Aminophylline 345-78-8, Pseudoephedrine hydrochloride 364-62-5, Metoclopramide 466-99-9, Hydromorphone 471-34-1, Calcium carbonate, biological studies 486-12-4, Triprolidine 554-10-9, 3-Iodo-1,2-propanediol 562-10-7, Doxylamine 586-06-1, Metaproterenol 606-04-2, Pamabrom 616-91-1, N-Acetylcysteine 642-72-8, Benzydamine 791-35-5, Chlophedianol 915-30-0, Diphenoxylate 2451-01-6, Terpin hydrate 3572-43-8, Bromhexine 3964-81-6, Azatadine 5104-49-4, Flurbiprofen 7020-55-5, Clidinium 7683-59-2, Isoprenaline 8024-48-4, Casanthranol 8050-81-5, Simethicone 12125-02-9, Ammonium chloride, biological studies 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate 15307-86-5, Diclofenac 15687-27-1 16958-94-4 18053-31-1, Fominoben 18559-94-9, Albuterol 18683-91-5, Ambroxol 21645-51-2, Aluminum hydroxide (Al(OH)3), biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutaline 25523-97-1,

09841025

Dexchlorpheniramine 27203-92-5, Tramadol 29679-58-1, Fenoprofen  
29975-16-4, Estazolam 30392-40-6, Bitolterol 33005-95-7, Tiaprofenic  
acid 34580-13-7, Ketotifen 35719-43-8 36322-90-4, Piroxicam  
36950-96-6, Cicloprofen 38194-50-2, Sulindac 41340-25-4, Etodolac  
42924-53-8, Nabumetone 50679-08-8, Terfenadine 51481-61-9, Cimetidine  
51803-78-2 53179-11-6, Loperamide 53716-49-7, Carprofen 57644-54-9,  
Bismuth subcitrate 61869-07-6, Domiodol 66357-35-5, Ranitidine  
68844-77-9, Astemizole 71125-38-7, Meloxicam 73590-58-6, Omeprazole  
74103-06-3, Ketorolac 74978-16-8, Magaldrate 75970-99-9, Norastemizole  
76824-35-6, Famotidine 76963-41-2, Nizatidine 79794-75-5, Loratidine  
80937-31-1, Flosulide 82626-48-0, Zolpidem 83799-24-0,  
Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine  
87848-99-5, Acrivastine 169590-42-5, Celecoxib 180200-68-4  
209967-47-5 209967-48-6 209967-50-0 209967-51-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(pharmaceutical compns. contg. acetaminophen salts and other drugs)